

Purpose: Despite improved staging and operative techniques, rate of incomplete resection (R1) of NSCLC has remained significant over the last decades. Patients with R1 resection have significantly worse survival compared to those with complete resection (R0). SBRT delivers high dose radiotherapy (RT) to tumours, in a short time (1-10 treatments), with high precision while sparing normal organs. The efficacy of SBRT in treating small lung tumours is documented but its use as neo-adjuvant therapy in LA-NSCLC is not reported yet. We hypothesized that a short course of pre-operative SBRT can be done safely and could improve rates of R0 resection of LA-NSCLC and conducted a Phase I trial (LINNEARRE I) to investigate the safety and feasibility of delivering, timely, neo-adjuvant SBRT in operable patients with LA-NSCLC at risk for positive resection margins.

Methods and Materials: Twenty appropriately staged (PET-CT/MRI and mediastinal staging) patients with biopsy proven T3-T4, N0-1, M0 NSCLC will be enrolled. Patients would be deemed medically operable by the surgical team but at risk of < R0 resection (due to invasion of mediastinal or hilar structures, chest wall or vertebral bodies). Primary outcome is feasibility i.e. the ability to complete SBRT as planned and proceed to surgery (Sx) within six weeks. Secondary outcomes include acute and late adverse events, R0/R1/R2 rates and secondary surrogates of feasibility. SBRT is delivered in over two weeks (in 10 fractions). Dose is escalated from 35 Gy to 50 Gy. Five patients will be accrued to each dose level of 35, 40, 45 and 50 Gy. At the latter dose level, normal tissue (nt) BED (133 Gy) exceeds that delivered concurrently with chemotherapy with 63-66 Gy/30 fractions (107-110 Gy) but is similar to that delivered by recent dose-escalation chemo-RT (74 Gy) studies. Clinical target volume (CTV) includes only the area of tumour deemed at risk of incomplete resection expanded by 3-5 mm into surrounding tissues where there is clinical suspicion of invasion.

Results: This study opened to accrual in late 2015. Dosimetric feasibility was tested in virtual plans of selected eligible cases that were planned to receive treatment at the highest planned dose level (50 Gy). All cases met dosimetric constraints for planned target volume (PTV) and organs at risk (OAR: great vessels, heart, esophagus, and proximal bronchi). Examples of virtual plans will be illustrated.

Conclusions: This is the first study to investigate SBRT as a neo-adjuvant therapy in LA-NSCLC. Virtual plans suggest that is feasible to deliver neoadjuvant SBRT safely to tumour volumes at risk for positive margins. A key aim of this study is to examine the adaptation of workflow in a Canadian academic institution to achieve timely neoadjuvant SBRT delivery. If successful this Phase I study will lead to further evaluation of pre-operative SBRT in LA-NSCLC, to help achieve improved rates of complete resection and improved outcomes.

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LIMITING CHEST WALL TOXICITY BY ADAPTING THE DOSE SCHEDULE AND DOSE CONSTRAINTS IN SBRT FOR EARLY-STAGE LUNG CANCER

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Purpose: Chest wall (CW) toxicity (rib fracture and/or pain) is a well-known complication after stereotactic body radiotherapy (SBRT) for early-stage lung cancer. The aim of this study is to evaluate the frequency of CW toxicity following SBRT and to determine the dosimetric parameters that influence the risk of CW toxicity.

Methods and Materials: We reviewed medical charts and radiotherapy (RT) plans from patients treated for T1 or T2N0 peripheral primary lung cancer between 2009 and 2015. Treatment was delivered by Cyberknife®, helical tomotherapy or using volumetric modulated arc therapy. CW structure corresponded to a 3 cm expansion of the lung excluding the lung volume. The median total dose delivered to the planning target volume was 60 Gy (range, 54- 60). SBRT was delivered in 3 fractions for patients with a CW V30 of less than 30cc. If the CW

V30 exceeded 30cc, 5 fractions were delivered and the SBRT plan was optimized on the biologically equivalent parameter of CW V30: CW V37 < 30 cc. We studied the association between CW toxicity and delivered dose using the Student T-test.

Results: Three hundred and eighty-one lesions were treated in a cohort of 363 patients with a median follow up of 17 months (range, 1 - 62). Twenty patients (6 %) had CW toxicity: 13 patients (4%) developed CW pain and nine patients (3%) developed rib fractures. For patient treated in 3 fractions, the mean CW V30 was 21 cc for patients with CW toxicity and 16 cc for patients without toxicity ($p < 0.05$). For patients treated in 5 fractions ($n = 55$), the small number of patients with chest wall toxicity did not allow comparison of V37 between groups. The CW V37 was inferior to 30 cc for all patients. CW toxicity rates were similar in the 3 or 5 fractions group (6% versus 4%). The two-year local control was similar in the two groups (96% versus 94%).

Conclusions: This study confirms that CW V30 is significantly associated with CW toxicity. When the CW V30 is greater than 30 cc, delivering SBRT in 5 fractions and with a CW V37 of less than 30 cc can limit CW toxicity without compromising tumour control.

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IS IT TIME FOR ADJUVANT CHEMOTHERAPY AFTER SBRT OF EARLY-STAGE NON-SMALL CELL LUNG CANCER?

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Purpose: Surgery remains the standard treatment for medically operable patients with early-stage non-small cell lung carcinoma (NSCLC). Adjuvant chemotherapy is routinely recommended following resection of tumours > 4 cm. For patients who decline surgery or are medically unfit, stereotactic body radiation therapy (SBRT) has emerged as an excellent alternative. The benefit of adjuvant chemotherapy following lung SBRT has not been studied. To evaluate the potential benefit of such a treatment, we reviewed the outcomes of T2N0 patients treated with SBRT.

Methods and Materials: We reviewed patients treated with SBRT for primary early-stage NSCLC between 2009 and 2015. Total target doses were between 50 and 60 Gy, administered in 3 - 8 fractions. All patients had a staging FDG PET/CT and histologic confirmation was obtained whenever possible (70 %). Mediastinal staging (MS) was performed if lymph node involvement was suspected on CT or PET/CT. Survival outcomes were estimated using the Kaplan-Meier method.

Results: Among the 556 NSCLC early stage patients treated with SBRT, 115 patients were staged T2N0. In T2N0 patients, the mean lesion size was 3.4 cm (range, 3 - 4.6cm). The one-year and three-year overall survival were 88% and 68% for patients with T2 disease, compare to 95% and 80% for the T1N0 patients ($p < 0.05$). The median disease-free survival was higher in the T1N0 group (48 versus 32 months). For T2N0 patients, the one-year and three-year local control rates were 98% and 91% respectively. Twenty patients (16.5%) presented a relapse, amongst which 16 (80%) were nodal or distant. The median survival of T2N0 patient post-relapse was 20 months.

Conclusions: Lung SBRT provided high local control rates, even for larger tumours. Overall survival and patterns of failure are similar to surgery. It remains to be seen if SBRT patients will be fit for and accepting of adjuvant chemotherapy but these results raise the question if adjuvant treatment is advisable post SBRT.

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DOES EARLY TUMOUR REGRESSION OBSERVED ON CONE-BEAM COMPUTED TOMOGRAPHY DURING CHEMO-RADIOOTHERAPY PREDICT FAVOURABLE OUTCOME IN LOCALLY ADVANCED LUNG ADENOCARCINOMA?

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